

ABSTRACT OF THE DISCLOSURE

Large-scale packaging of alphavirus replicons is accomplished by co-transfecting host cells with three RNA molecules: (1) an alphavirus replicon comprising a sequence
5 encoding a heterologous protein; (2) a helper RNA encoding a capsid protein and (3) a helper RNA encoding two alphavirus glycoproteins. The helper RNAs contain cis-acting elements that allow efficient replication of the helper RNAs and their packaging
10 into viral particles as well as packaging of replicon genomes. These populations of viral particles can be propagated at high titers in cell culture by infecting cells at high multiplicity. Propagation of packaged replicons at an escalating scale is useful for large-scale production of recombinant proteins and/or vaccine.